

WHAT IS CLAIMED IS:

1. A method of amplifying a 5kb or longer subsequence of a target nucleic acid in an aqueous solution using a polymerase chain reaction, the method comprising:

(i) contacting the target nucleic acid with a protein comprising at least two heterologous domains, wherein a first domain that is a sequence-non-specific nucleic-acid-binding domain is joined to a second domain that is a polymerase domain with error-correcting activity, where the sequence non-specific nucleic-acid-binding domain:

(a) binds to double-stranded nucleic acid, and

(b) enhances the processivity of the polymerase compared to an identical polymerase not having the sequence non-specific nucleic-acid-binding domain fused to it, and

wherein the solution is of a composition that permits the binding domain to bind to the target nucleic acid and the polymerase domain to extend a primer that is hybridized to the target nucleic acid sequence to a length of 5 kb or longer;

(ii) incubating the solution using a polymerase chain reaction temperature profile that amplifies the 5 kb or longer subsequence.

2. A protein of claim 1 wherein the nucleic-acid-modifying domain has thermally stable polymerase activity.

3. A protein of claim 1 wherein the nucleic-acid modifying domain comprises a *Pyrococcus* polymerase domain.

4. A method of claim 1 wherein the sequence-non-specific nucleic-acid-binding domain specifically binds to polyclonal antibodies generated against either Sac7d or Sso7d.

5. A method of claim 1 wherein the sequence-non-specific nucleic-acid-binding domain contains a 50 amino acid subsequence containing 50% amino acid similarity to Sso7D.

6. A method of claim 1 wherein the sequence-non-specific nucleic-acid-binding domain specifically binds to polyclonal antibodies generated against Sso7d.

7. A method of claim 1 wherein the sequence-non-specific nucleic-acid-binding domain is Sso7d.

8. A method of amplifying a subsequence of a target nucleic acid in an aqueous solution using a polymerase chain reaction, the method comprising:

(i) contacting the target nucleic acid with a protein comprising at least two heterologous domains, wherein a first domain that is a sequence-non-specific nucleic-acid-binding domain is joined to a second domain that is a polymerase domain with error-correcting activity, where the sequence non-specific nucleic-acid-binding domain:

(a) binds to double-stranded nucleic acid, and

(b) enhances the processivity of the polymerase compared to an identical polymerase not having the sequence non-specific nucleic-acid-binding domain fused to it, and

wherein the solution comprises 10^5 or fewer copies/ml of the target nucleic acid and is of a composition that permits the binding domain to bind to the target nucleic acid and the polymerase domain to extend a primer that is hybridized to the target nucleic acid sequence;

(ii) incubating the solution using a polymerase chain reaction temperature profile that amplifies the subsequence.

9. A protein of claim 8 wherein the nucleic-acid-modifying domain has thermally stable polymerase activity.

10. A protein of claim 8 wherein the nucleic-acid modifying domain comprises a *Pyrococcus* polymerase domain.

11. A method of claim 8 wherein the sequence-non-specific nucleic-acid-binding domain specifically binds to polyclonal antibodies generated against either Sac7d or Sso7d.

12. A method of claim 8 wherein the sequence-non-specific nucleic-acid-binding domain contains a 50 amino acid subsequence containing 50% amino acid similarity to Sso7D.

13. A method of claim 8 wherein the sequence-non-specific nucleic-acid-binding domain specifically binds to polyclonal antibodies generated against Sso7d.

14. A method of claim 8 wherein the sequence-non-specific nucleic-acid-binding domain is Sso7d.

09870353 053001
T00E50" E5E02B60